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Reply to: Sodium nitroprusside for schizophrenia: Could methodological variables account for the different results obtained?

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We thank Maia-de-Oliveira and colleagues for their thoughtful comments on our recent paper (Stone et al. 2016). There were indeed differences in the population of patients studied in our study and in their original investigation (Hallak et al. 2013). We noted in our paper that the sample studied by Hallak and colleagues were younger and had a shorter duration of illness than the patients in our study. We recognise that the response to pharmacological treatment in schizophrenia may vary with stage of illness, and we are currently running a study of a nitric oxide donor compound in patients with first episode psychosis to investigate this possibility. Given the high prevalence of tobacco use in patients with schizophrenia (Hartz et al 2014), the suggestion that smoking may influence the efficacy of SNP is interesting, and merits further study, as does the possibility that the response may vary across different ethnic groups.

Hallak JE, Maia-de-Oliveira JP, Abrao J, Evora PR, Zuardi AW, Crippa JA, Belmonte-de-Abreu P, Baker GB, Dursun SM (2013). Rapid improvement of acute schizophrenia symptoms after intravenous sodium nitroprusside: a randomized, double-blind, placebo-controlled trial. *JAMA Psychiatry* **70**, 668–676.

Hartz SM, Pato CN, Medeiros H, Cavazos-Rehg P, Sobell JL, Knowles JA, Bierut LJ, Pato MT; Genomic Psychiatry Cohort Consortium (2014). Comorbidity of severe psychotic disorders with measures of substance use. *JAMA Psychiatry* **71(3)**, 248-54.

Stone JM, Morrison PD, Koychev I, Gao F, Reilly TJ, Kolanko M, Mohammadinasab A, Kapur S, McGuire PK (2016). The effect of sodium nitroprusside on psychotic symptoms and spatial working memory in patients with schizophrenia: a randomized, double-blind, placebo-controlled trial. *Psychological Medicine* **22**, 1-8.